

Hepcidin—Ferroportin: *Partners in Iron Balance*

To ensure that we have an adequate but not overly abundant or excessive supply of iron, humans have intricate systems that maintain iron homeostasis, which is the body's ability to regulate its inner environment for iron stability. Iron homeostasis is influenced by the status of iron stores; hemoglobin levels; red blood cell production (erythropoiesis) and red cell destruction (hemolysis); or inflammation (immune response).

In an iron disorder, one or more of these components is out of balance. Iron levels are generally determined by measuring hemoglobin (functional iron), transferrin-iron saturation percentage (TS%)—(iron in transport) and serum ferritin (SF)—iron in containment/storage. Therapy for any iron disorder and prediction of response to therapy often is based on these values, which must be interpreted carefully. Take for example, iron deficiency anemia (IDA); in true IDA all of these levels will be low. Whereas, in anemia of chronic disease (anemia of inflammatory response), the hemoglobin and TS% will be low, but the serum ferritin will be elevated. If only hemoglobin is measured the two anemias look alike; one may benefit from iron supplements—whereas the other can result in harm if iron supplements are taken.

Two substances are integral to the body's natural iron regulating systems, hepcidin and ferroportin. Together they regulate the exit or outflow of iron through cells. Their activity influences various states of iron overload and anemia.

Hepcidin was first described in 2000 and later given its name because of two characteristics: “hep” because it is produced in the liver (hepatic) and “cidin” because of its antimicrobial capabilities.

Hepcidin suppresses ferroportin. The function of ferroportin is to serve as a channel through which

iron is transported across the cell membrane into plasma. Thus elevated hepcidin impedes iron transit.

Imbalances of hepcidin and ferroportin increase the risk of disease. Elevated serum ferritin is a result rather than the cause of an imbalance. Conditions known to have such imbalances include:

- hemochromatosis (all known types);
- thalassemia;
- sickle cell disease;
- iron deficiency anemia—a) acquired by diet or blood loss and responsive to iron supplementation or b) inherited where the response to iron supplementation is poor—referred to as a refractory iron deficiency anemia (IRIDA);
- viral hepatitis;
- metabolic syndrome (possibly atherosclerosis); and
- cancer

Iron dysregulation may contribute to bad disease outcome in various cancers. In one US study investigators at Wake Forest University School of Medicine noted that ferroportin and hepcidin are expressed in breast tissue (epithelial cells). They examined more than 800 breast cancer tissue samples and reported that ferroportin is greatly reduced in breast cancer cells compared to non-malignant breast tissue. These investigators concluded that high ferroportin and low hepcidin gene expression in cancer cells may result in as much as a 90% chance of doubling survival from 5 years to 10 years.

Iron is also dysregulated in various endocrine (glandular) disorders. In a study conducted at one university hospital in Spain, hepcidin and ferroportin levels were measured in 34 women with polycystic ovarian syndrome (PCOS) and elevated androgen levels. The findings were compared to 30 women without elevated levels of androgen. Investigators demonstrated that

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women with PCOS had decreased hepcidin and increased serum ferritin compared with women without PCOS. Furthermore, women with PCOS and infrequent or very light menstruation, (oligoamenorrhea) where less iron is lost through menstruation, showed decreased hepcidin levels with increased serum ferritin levels.

Presently tests are available to detect hepcidin levels, but there is no economical way to test ferroportin levels. Besides, knowing these levels simply reveals a risk rather than provides a prognosis. It seems more reasonable and cost effective for everyone to know his or her iron levels and aim to keep these levels in balance with diet, blood donation or iron replenishment when warranted.

This chart is for information purposes only and not meant to provide a diagnosis.

iron panel	Comparing Iron Test Results				
	Serum Iron	Serum Ferritin	Transferrin Iron Saturation Percentage (TS%)	Hemoglobin	Hepcidin
Hemochromatosis/ Iron overload	↑	↑	↑	Normal	↓
Juvenile Hemochromatosis	↑	↑	↑	Normal	↓ ↓
Transfusional Iron overload	↑	↑	↑	↓	↑
Anemia of Inflammatory Response	↓	↑ <small>OR NORMAL</small>	↓	↓	↑
Iron Deficiency Anemia (IDA) acquired: bleeding or diet	↓	↓	↓	↓	↓
Iron-refractory Deficiency Anemia (IRIDA)	↓	↓	↓	↓	↑

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